CHAMPVA POLICY MANUAL

CHAPTER: 2
SECTION: 31.10
TITLE: HIGH DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION

AUTHORITY: 38 CFR 17.270(a), 17.272(a)(1)(4)(13)(14)(59), and 17.273

RELATED AUTHORITY: 32 CFR 199.4(e)(5) and (g)(15)

I. EFFECTIVE DATE

A. November 1, 1983, for high-dose chemotherapy (HDC) with allogeneic bone marrow transplants using related donors.

B. May 1, 1987, for HDC with autologous bone marrow transplant (ABMT) or peripheral stem cell therapy (PSCT) for Hodgkin's disease, non-Hodgkin's lymphoma and neuroblastoma.

C. November 1, 1987, for HDC with ABMT or PSCT for acute lymphocytic and nonlymphocytic leukemias.

D. July 1, 1989, for HDC with allogeneic bone marrow transplants using unrelated donors.

E. January 1, 1994, for HDC with AMBT or PSCT for chronic myelogenous leukemia.

F. January 1, 1994, for HDC with ABMT and PSCT for Wilms' tumor.

G. January 1, 1995, for ABMT for hypereosinophilic syndrome.

H. October 1, 1995, for HDC with ABMT or PSCT for metastatic breast cancer.

I. January 1, 1996, for AMBT using related 3 antigen mismatch donors for patients with undifferentiated leukemia, chronic myelogenous leukemia (CML), aplastic anemia, acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML).

J. January 1, 1996, for HDC with ABMT or PSCT for Waldenstrom's macroglobulinemia.

K. July 11, 1996, for HDC with ABMT or PSCT for multiple myeloma.

L. August 1, 1996, for allogenenic umbilical cord blood transplants.

M. October 1, 1996, for HDC with AMBT or PSCT for amyloid light-chain (AL) amyloidosis.

N. May 1, 1997, for HDC with ABMT or PSCT for trilateral retinoblastoma/pineoblastoma.

O. September 2, 2002, for agnogenic myeloid metaplasia (myelofibrosis).

II. PROCEDURE CODE(S)

38230, 38231, 38240, 38241, 86812-86822, and 88240-88241

III. DESCRIPTION

A. High dose chemotherapy (HDC) as the use of cytotoxic therapeutic agents (that are otherwise approved for general use in humans by the Food and Drug Administration (FDA) in dosages and/or frequencies of dosage that exceed the FDA labeling for the agent. HDC is generally considered when conventional regimens of chemotherapeutic agents have failed to arrest disease progression. One of the major adverse effects of HDC is that of bone marrow suppression, itself a potentially lethal process.

B. Stem cells are multipotential, blood-cell producing agents important in immune defenses against disease. Stem cell "transplantation" or "rescue" is defined as a technique for collecting stem cells from a donor (either from the bone marrow or from the bloodstream), preparing and storing the collected stem cells, then reinfusing the prepared stem cells into the bloodstream of a patient in the treatment of oncologic, hematologic or lymphoproliferative disease with curative potential. The goal of stem cell "transplantation" or "rescue" is to reverse the bone marrow suppression caused by either HDC or by a primary bone marrow disease process, (e.g., aplastic anemia). The four general types of stem cell "transplantation" or "rescue" are addressed below.

C. There are four general types of stem cell “transplantation” or “rescue”:

1. Allogeneic bone marrow transplantation (BMT), where stem cells from a histocompatible donor (other than the patient) are harvested, then later infused into the bloodstream of the patient. With BMT, the patient may have either a related or unrelated donor who has the same or closely matched human leukocyte antigen (HLA) typing necessary for successful transplantation.

2. Autologous bone marrow transplant (ABMT), where the patient is both donor and recipient of stem cells harvested from the bone marrow.

3. Peripheral stem cell therapy (PSCT), where the patient is both donor and recipient of stem cells harvested from the bloodstream using the apheresis process. This technique is generally reserved for those patients who have disease involvement of their bone marrow, making ABMT less satisfactory.

4. Umbilical cord blood stem cell transplantation (UCBT), where stem cells are harvested from the umbilical cord and placenta, then later infused into the bloodstream of the patient.

IV. POLICY

A. Benefits are allowed for HDC with ABMT or PSCT and allogenic stem cell transplantation with or without HDC for the following:

1. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, or myelomonoblastic).

2. AL (amyloid light-chain) amyloidosis.

3. Chronic myelogenous leukemia.

4. Glioblastoma (a malignant, fast growing tumor) multiform.

5. Gliofibromas (also known as desmoplastic astrocytoma and desmoplastic glioblastoma).

6. Multiple myeloma.

7. Neuroblastoma, Stage III or IV, when the patient is one for who further treatment with a conventional dose therapy is not likely to achieve a durable remission.

8. Non-Hodgkin’s lymphoma, intermediate or high-grade, and Hodgkin’s disease when:

a. Conventional dose chemotherapy has failed.

b. The patient has relapsed following a course of radiation therapy, and has also failed at least one course of conventional dose chemotherapy subsequent to the failed radiation therapy.

c. In the case of ABMT, the patient has adequate marrow function and no evidence of marrow involvement with lymphoma.

Note: For purposes of CHAMPVA coverage, mantle cell lymphomas will be considered as intermediate grade, non-Hodgkin's lymphomas.

9. Posterior fossa teratoid brain tumors.

10. Primitive neuroectodermal tumors (PNET)/Ewing's Sarcoma.

11. Rhabdomyosarcoma and undifferentiated sarcomas when the medical record documents that the patient has failed the course of therapy recommended by the Intergroup Rhabdomyosarcoma Study.

12. Stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body and that has relapsed after responding to first-line treatment. Stage IV metastatic or primary breast cancer that has spread to other sites of the body in patients who have not been previously treated with systemic therapy for metastic disease. Stage IV metastatic or primary breast cancer that has spread to other sites of the body and that is responding to primary systemic therapy. (This does not include primary disease in men. Benefits may be allowed for male patients with stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body subject to the same provisions as noted above.)

13. Trilateral retinoblastoma/pineoblastoma.

14. Waldenstrom's macroglobulinemia.

15. Wilms' tumor.

B. Allogenic stem cell transplantation, with or without HDC is covered in the treatment of the following disease processes when either a related or unrelated donor is used:

1. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, myelomonoblastic), chronic myelogenous leukemia (CML), or preleukemic syndromes.

a. Partially matched related donor stem cell transplantation is covered for patients with acute lymphoblastic leukemia (ALL) with a 2-antigen mismatch during the second or third remission.

b. Treatment with unirradiated donor lymphocytes (buffy coat) is covered for CML patients who relapse following their first or subsequent course of HDC with allogeneic BMT. The medical record must document that the patient:

(1) is in relapse following an adequate trial of HDC with allogeneic BMT for CML.

(2) is qualified (or would have qualified) for authorization for HDC with allogeneic BMT according to the provisions set forth in this policy.

3. Amegakaryocytic thromboyctopenia.

4. Anogenic myeloid metaplasia (myelofibrosis).

5. Aplastic anemia.

6. Chronic lymphocytic leukemia (CLL) when previous therapy has failed or when the CCL is refractory to conventional therapy.

7. Chronic granulocytic leukemia (CGL)

8. Chronic myelogenous leukemia

9. Congenital amegakaryocytic thrombocytopenia.

10. Congenital mucopolysaccharidoses.

11. Hypereosinophilic syndrome.

12. Hodgkin's Lymphoma for Stage III or IV A or B patients who are either in relapse, or refractory to primary chemotherapy.

13. Follicular non-Hodgkin's Lymphoma for patients who have failed primary therapy.

14. Infantile malignant osteopetrosis (Albers-Schonberg syndrome or marble bone disease).

15. Intermediate and high grade lymphoma with bone marrow involvement.

16. Kostmann's Syndrome (severe infantile agranulocytosis).

17. Leukocyte adhesion deficiencies.

18. Metachromatic leukodystrophy.

19. Mucolipidoses (Gaucher's, metachromic leukodystrophy, etc.)

20. Myelodysplasia/myelofibrosis for patients with refractory anemia (idiopathic, or secondary to drug or toxin exposure), who have an HLA-identical donor. Patients must have one or more of the following:

a. excess blasts or excess blasts in transformation,

b. chronic myelomonocytic leukemia, or

c. increasing blast counts or ringed sideroblasts with at least one of the following, neutropenia, thrombocytopenia or chromosomal abnormalities.

21. Myeloproliferative/dysplastic syndromes.

22. Mucopolysaccharidosis (Hunter's, Hrler's, etc.)

23. Non-Hodgkin's lymphoma when:

a. Stage III or IV A or B, intermediate and high-grade NHL in second or subsequent clinical remission.

b. Stage IV A or B, high-grade NHL with a lymphoma mass over 10 cm and with more than one involved extranodal site, in first clinical remission, because these patients have such a high likelihood of recurrence.

24. Severe combined immunodeficiency, e.g., adenosine deaminase deficiency and idiopathic deficiencies.

a. Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens) in determining histocompatibility in the treatment of Bare Lymphocyte Syndrome.

b. Unrelated donor and/or related donor (without regard for mismatched antigens) with or without T cell lymphocyte depletion in the treatment of familial erythrophagocytic lymphohistiocytosis (FEL); generalized lymphohistiocytic infiltration; familial lymphohistiocytosis; familial reticuloendotheliosis; familial hemophagocytic lymphohistiocytosis (FHL); for patients whose medical records document failure of conventional therapy (etoposide; corticosteroids; intrathecal methotrexate; and cranial irradiation).

c. Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens) in the treatment of X-linked severe combined immunodeficiency syndrome (X-Linked SCID).

25. Sickle cell disease.

26. Thalassemia major.

27. Wiskott-Aldrich syndrome.

28. X-linked lymphoproliferation syndrome.

C. Unirradiated donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion or donor monomuclear cell infusion) is covered for patients with CML, who relapse following their first or subsequent course of HDC with allogeneic BMT. The medical record must document that the patient:

1. Is in relapse following an adequate trial of HDC with allogenic BMT or CML.

2. Is qualified (or would have qualified) for authorization for HDC with allogeic BMT according to the provisions set forth in this policy.

D. Allogeneic umbilical cord blood transplantation, with or without HDC, is covered for children and adolescents in the treatment of the following disease processes when either a related or unrelated donor is used. The following list of conditions is not all-inclusive. Those conditions for which this procedure can be documented as medically necessary, appropriate and the standard of care may also be covered.

1. Acute lymphocytic or non-lymphocytic leukemias.
2. Adrenoleukodystrophy.
3. Aplastic anemia.
4. Blackfan-Diamond anemia.
5. Chronic myelogenous leukemia.
6. Congenital amegakaryocytic thrombocytopenia.
7. Fanconi anemia.
8. Globoid cell leukodystrophy.
9. Hurler syndrome.
10. Hunter syndrome.
11. Infantile malignant osteopetrosis.
12. Intermediate and high grade non-Hodgkin's Lymphoma.
13. Kostmann's syndrome.
14. Lesh-Nyhan disease.
15. Myelodysplastic syndrome.
16. Neuroblastoma.
17. Non-Hodgkin's lymphoma.
18. Severe combined immunodeficiency.
19. Sickle cell anemia.
20. Thalassemia major.
21. Wiskott-Aldrich syndrome.

22. X-linked lymphroproliferative syndrome.

E. Syngeneic (identical twin donor) stem cell transplantation is covered for the treatment of Hodgkin's disease.

F. In those allogenic stem cell transplantation cases in which it has been established that a related donor is not possible, and when the only alternative is an unrelated donor, benefits may be extended only under the following conditions:

1. The patient must use the National Marrow Donor Program (NMDP) for donor searches. (The NMDP is located in Minneapolis, Minnesota, 1-800-654-1247, and is available to anyone needing assistance in locating a suitable donor for unrelated allogeneic bone marrow transplantation). Donor searches through foreign registries must first be initiated or coordinated through NMDP. Prior to using NMDP services, preauthorization for services must be obtained from the Health Administration Center (HAC).

2. Donor matching must meet the criteria established by the NMDP for identical and mismatched typing (refer to paragraph E. of this policy).

3. Requests for a donor search must be initiated and coordinated through the NMDP, and the transplant must be performed at one of its NMDP certified centers.

4. CHAMPVA will reimburse costs for donor searches only when the search has been initiated and coordinated by the NMDP.

a. Charges for donor searches must be fully itemized and billed by the transplant center.

b. Costs for donor searches will be cost shared in accordance with established reimbursement guidelines for outpatient diagnostic testing.

c. Donor search costs may be billed at any time. There is no limit on how many searches a transplant center may request from the search printout.

G. Histocompatibility criteria.

In cases where related donor matches are not perfect, e.g., the histocompatibility is less than an identical antigen match, the same criteria and standards for typing mismatched unrelated donors must be used.

a. For the purposes of the National Marrow Donor Program and CHAMPVA coverage, the greatest degree of incompatibility allowed between donor or recipient (for either related or unrelated donors) is a single antigen mismatch at the A, B, or Dr. locus, except for:

(1) Patients 18 years or younger with relapsed luekemia, when histocompatible related or unrelated donors are not available, parental CD34++stem cell transplantation with 2-3 antigen mismatch is allowed.

(2) Patients with undifferentiated leukemia, chronic myelogenous leukemia (CML), aplastic anemia, acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML), when histocompatible related or unrelated donors are not available, a 3 antigen mismatch is allowed for related donors.

(3) Patients with acute lymphoblastic leukemia (ALL) where a 2 antigen mismatch is allowed for related donors.

b. Donor searches accomplished through foreign registries must meet the same typing criteria as established by the NMDP (refer to paragraph D. above).

c. DNA-HLA tissue typing to determine histocompatibility is covered.

H. Benefits for stem cell and umbilical cord blood stem cell harvesting:

1. Benefits will not be allowed for stem cell harvesting and/or cryopreservation and umbilical cord blood stem cell harvesting and/or cryopreservation until the stem cell reinfusion has been completed. In the event that the patient expires prior to the stem cell reinfusion being completed, benefits for the harvesting may be allowed.

2. Charges for stem cell and umbilical cord blood preparation and storage shall be billed through the transplantation facility in the name of the CHAMPVA patient.

3. Charges for the umbilical cord blood bank may be allowed only for patients who have undergone a covered transplant.

I. Benefits are allowed for hepatitis B pneumococcal vaccines for transplant patients.

V. POLICY CONSIDERATIONS

A. Preauthorization and retrospective authorization for HDC with ABMT or PSCT, and HDC with allogeneic BMT must meet the following two criteria:

1. The patient meets (or as of the date of transplantation, would have met) patient selection criteria.

2. The transplant facility is (or as of the date of transplantation would have been) Medicare, TRICARE, or VA approved.

B. In those cases where the beneficiary fails to obtain preauthorization, benefits may be extended if the services or supplies otherwise would qualify for benefits but for the failure to obtain preauthorization. If preauthorization is not received, the Health Administration Center will review the claim to determine whether the beneficiary's condition meets the clinical criteria for the transplantation.

C. Claims for services and supplies related to the transplant for patients under the age of 18 will be reimbursed on billed charges. Claims for HDC and transplants for adult patients, 18 years and older, will be reimbursed under the DRG payment system. Outpatient institutional facility charges will be paid as billed. Professional services are reimbursed based on CMAC.

D. Donor costs are payable under the conditions as outlined within Chapter 2, Section 31.1, *Donor Costs*.

E. Air ambulance may be cost shared when determined to be medically necessary (see Chapter 2, Section 32.1, *Ambulance Service*).

VI. EXCEPTIONS

If the patient otherwise meets the coverage criteria for HDC with ABMT as listed in POLICY above, harvesting of the required stem cells by apheresis from peripheral blood, i.e., PSCT, rather than bone marrow, may be allowed.

VII. EXCLUSIONS

A. Administration of a drug that is not FDA approved (see Chapter 2, Section 3.4, *Immunotherapy for Malignant Disease*).

B. Allogeneic BMT or PSCT with HDC for treatment of multiple myeloma.

C. Allogeneic bone marrow transplantation for neuroblastoma.

D. Allogeneic donor BMT (infusion) performed with or after organ transplants for the purpose of increasing tolerance of the organ transplant.

E. Allogeneic peripheral stem cell transplantation for non-Hodgkin's lymphoma.

F. Allogenic stem cell transplant for:

1. chronic lymphocytic leukemia (CLL)

2. ovarian cancer.

3. small lymphocytic lymphoma (SLL)

4. solid tumors.

5. polycythemia vera.

G. Allogenic bone marrow transplants using unrelated donors.

H. Autologous umbilical cord blood transplantation therapy.

I. Donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion, and donor mononuclear infusion) if not specifically listed as covered above.

J. HDC with or without ABMT, HDC with or without PSCT, or HDC with or without allogeneic BMT, if not specifically listed as covered in paragraphs A and B under POLICY above.

K. HDC with ABMT or PSCT or HDC with allogeneic BMT if the patient has a concurrent condition (other existing illness) that would jeopardize the achievement of successful transplantation.

L. HDC with ABMT or PSCT for treatment of low-grade non-Hodgkin's lymphoma. Allogeneic bone marrow transplantation for treatment of low-grade non-Hodgkin's lymphoma is not a benefit.

M. HDC with allogeneic BMT for the treatment of Hodgkin's disease. This does not include syngeneic stem cell transplantation which is covered for the treatment of Hodgkin's disease.

N. HDC with ABMT or PSCT for:

1. treatment of desmoplastic small round-cell tumor.

2. treatment of non-metastatic breast cancer.

3. treatment of yolk-sac tumor (endodermal sinus tumor).

O. HDC with allogeneic BMT for treatment of Waldenstom's macroglobulinemia.

P. HDC with allogeneic stem cell transplantation for the treatment of cold agglutinin disease.

Q. HDC with stem cell rescue for:

1. ovarian cancer.

2. testicular cancer.

R. In-vitro stem cell processing (stem cell assay or purging).

S. Reduced intensity transplants (non-myeloablative allogenic stem cell transplants, mini transplants, transplant lite) for renal cancer and other solid tumors of solid tissues or organs.

T. Salvage high dose chemotherapy/allogenic stem cell support (HDC/AlloSCS) after high dose chemotherapy/autologous stem cell support (HDC/AuSCS) for patients with recurrent neuroblastoma, metastatic breast cancer, germ cell tumors in relapse or any other solid tumor.

U. Salvage HDC/AlloSCS for relapse of incomplete remission after HDC/AuSCS for patients with multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's lymphoma, acute myeloblastic leukemia and acute lymphoblastic leukemia.

V. Pre- or post-transplant nonmedical expenses (i.e., out-of-hospital living expenses to include, hotel, meals, privately owned vehicle for the beneficiary or family members). [38 CFR 17.272(a)(4)]

W. Services/supplies provided at no cost or if the beneficiary (or sponsor) has no legal obligation to pay. This includes expenses or charges that are waived by the transplantation center. [38 CFR 17.272 (a)(1)]

X. Services, supplies or devices, even those used in lieu of the transplantation, when determined to be related or integral to an experimental/investigational (unproven) procedure. [38 CFR 17.272(a)(14)]

Y. Services/supplies that are not provided in accordance with applicable program criteria (i.e., part of a grant or research program, unproven procedure). [38 CFR 17.272 (a)(13)]

Z. The transportation of a living donor or cadaver. [38 CFR 17.272(a)(59)]

END OF POLICY